

PATENT COOPERATION TREATY


PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

REC'D 14 MAR 2005

WIPO PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 429 WO		FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/DK2004/000283		International filing date (day/month/year) 23.04.2004	Priority date (day/month/year) 25.04.2003	
International Patent Classification (IPC) or national classification and IPC C07D209/08, C07D409/06, C07D401/06, C07D403/06, C07D407/06, C07D417/06, A61K31/404, A61P25/08				
Applicant H. LUNDBECK A/S et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 21.10.2004		Date of completion of this report 11.03.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Menegaki, F Telephone No. +49 89 2399-8277		



**INTERNATIONAL PRELIMINARY REPORT
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-103 as originally filed

Claims, Numbers

1-30 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	17-20, 22
	No: Claims	1-16,21,23-30
Inventive step (IS)	Yes: Claims	17-20,22
	No: Claims	1-16,21,23-30
Industrial applicability (IA)	Yes: Claims	1-30
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

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(V)

Having regard to the International Search Report the subject matter claimed differs from documents

(D1) WO 03/031409, in particular Examples 7,8,11 therein; (D3) WO 99/09024, in particular 4th compound on p.27 therein; (D4) Bioorganic & Med. Chem. Letters, vol.11(14), 2001, p.1907-1910, in particular compound 3 in T.1 therein, due to the disclaimer in Claim 1, excluding certain specific compounds.

(D2) WO 01/12187, in particular compounds 25,33,51,55,85 appear to be novelty destroying for present formula (I), since they are not covered by the disclaimed compounds. The provisions with regard to the definition of R^2/R^3 appear to have been introduced for the chemical stability of the compounds.

(D5) US-A-5234942, in particular col.56-59 therein, discloses **6-carboxylamino** substituted indole derivatives, differing further from the present compounds due to the definition of R^5 -substituent on the Y-group.

(D6) WO 02/066426 discloses fluorindol-2-one derivatives.

Moreover, it is noted that (D7) Journal of Enzyme Inhibition and Medicinal Chemistry, vol.18(2), 2003, p.89-94, which is a P-document not relevant at this stage, in particular compounds 7c-7h on p.93 therein, appears to fall within the scope of present formula (I).

The requirements of Art.33(2) PCT do not appear to be fulfilled for present Claims 1-16,21,23-30 with regard to (D2), whereas Claims 17-20, 22 appear to be novel.

The problem underlying the present invention appears to be the provision of **novel** compounds of formula (I) having KCNQ potassium channel opening properties. Claims 17-20, 22 appear to fulfil the requirements of Art.33(3) PCT, given the fact that documents (D1) to (D5) disclose different activities and Doc.(D6) discloses structurally essentially different KCNQ opening agents, which are not considered to be relevant in this respect. If novelty is restored, an inventive step could also be acknowledged for Claims 1-16, 21 and 23-30. Nevertheless, reference is made to the broadness of the claimed scope of formula (I) in said claims, and it is noted that substituent definitions R^1 , $R^{1'}$ are merely supported by hydrogen; "U" is not present in the examples ($s=0$); R^2 appears to be supported by phenyl(-alkyl), nitro and amino, and no R^2 and $R^{1'}$, or R^{10} and $R^{10'}$ forming a ring together are present. Accordingly, if novelty can be restored an inventive step could be acknowledged provided that all claimed compounds of formula (I) possess the claimed

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KCNQ opening properties.